

Refine Search

Search Results -

Terms	Documents
(lamellar adj1 bodies) same sphingomyelin	7

Database:

US Pre-Grant Publication Full-Text Database
 US Patents Full-Text Database
 US OCR Full-Text Database
 EPO Abstracts Database
 JPO Abstracts Database
 Derwent World Patents Index
 IBM Technical Disclosure Bulletins

Search:

L12



Search History

DATE: Wednesday, November 14, 2007 [Purge Queries](#) [Printable Copy](#) [Create Case](#)

Set Name Query

side by side

Hit Count Set Name

result set

DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR

<u>L12</u>	(lamellar adj1 bodies) same sphingomyelin	7	<u>L12</u>
<u>L11</u>	infasurf and sphingomyelin	13	<u>L11</u>
<u>L10</u>	infasurf same sphingomyelin	0	<u>L10</u>
<u>L9</u>	exosurf and sphingomyelin	47	<u>L9</u>
<u>L8</u>	exosurf same sphingomyelin	0	<u>L8</u>
<u>L7</u>	exosurf	116	<u>L7</u>
<u>L6</u>	L5 and otitis	0	<u>L6</u>
<u>L5</u>	(liposome adj5 sphingomyelin)	715	<u>L5</u>
<u>L4</u>	(liposome adj5 sphingomyelin) and (cystic adj1 fibrosis)	16	<u>L4</u>
<u>L3</u>	(liposome adj5 sphingomyeling) and (cystic adj1 fibrosis)	0	<u>L3</u>
<u>L2</u>	(lung adj1 surfactant) same sphingomyelin	23	<u>L2</u>
<u>L1</u>	(cystic adj1 fibrosis) same sphingomyelin	10	<u>L1</u>

END OF SEARCH HISTORY

[First Hit](#) [Fwd Refs](#)[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

End of Result Set



Generate Collection

Print

L2: Entry 23 of 23

File: USPT

Jan 26, 1982

DOCUMENT-IDENTIFIER: US 4312860 A

**** See image for Certificate of Correction ****

TITLE: Lung surfactant compositions

Brief Summary Text (8):

The chemical composition of "lung surfactant" has been investigated and the results have been published in a number of papers, e.g. Respiratory Distress Syndrome, Academic Press Inc., 1973, pp. 77-98. Such studies indicate that natural lung surfactant is a complex mixture of many components of which the major component is a lipid, dipalmitoyl phosphatidyl choline (according to current naming criteria more correctly, 1,2-dipalmitoyl-sn-3-glycerophosphoryl choline). Dipalmitoyl phosphatidyl choline, commonly abbreviated as DPPC, occurs in lung surfactant to the extent of about 41% by weight. Mixed monenoic lecithins make up about 25% by weight; cholesterol makes up about 9% by weight; mixed proteins about 9% by weight; phosphatidyl ethanolamine, about 5%; various glycerides and phosphatidyl serine and phosphatidyl glycerol, about 4%, respectively; lysolecithin, about 2%; with sphingomyelin and fatty acids, each about 1%. The above noted materials and %'s are for surfactant removed from canine lungs; however, the mix of materials and %'s generally hold true for the higher mammals. For instance, both bovine and human lung surfactant also comprise a similar mix, with DPPC running in the same range of approximately 40% by weight.

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

[First Hit](#) [Fwd Refs](#)[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

Generate Collection

Print

L2: Entry 18 of 23

File: USPT

Aug 22, 1995

DOCUMENT-IDENTIFIER: US 5443989 A

TITLE: Method for assessing fetal lung maturity using amniotic fluid samples

Brief Summary Text (5):

Immature fetal lungs lack an adequate surfactant layer which normally lines the alveoli and helps to keep the alveoli open after exhalation. The quantity of phospholipids generally in amniotic fluid, and of dipalmitoyl phosphatidyl choline (or "DPPC") in particular, has been correlated with the amount of surfactant lining the alveoli and with the degree of fetal lung maturity. Phosphatidyl choline (or "PC") fractional species represent nearly 80 percent of the surfactant phospholipid varieties in the fetal lung (Clements, Am. Rev. Resp. Dis, 101:984 (1970); and dipalmitoyl phosphatidyl choline (or "DPPC") constitutes about 60 percent of the fetal lung phosphatidyl choline species fraction. Other PC fraction species include 1-palmitoyl, 2-palmitoleoyl-PC (20%); 1-palmitoyl, 2-oleoyl-PC (10%); and other minor PC varietal species (10%). The remaining lung surfactant phospholipid components also include phosphatidyl inositol, phosphatidyl ethanolamine, sphingomyelin and phosphatidyl serine. Interestingly enough, the second major phospholipid of lung surfactants is phosphatidyl glycerol, comprising more than 10 percent of the mature surfactant in the lining of the lung (Pleger and Thomas, Arch. Intern. Med, 127:863 (1971); Hallman and Gluck, Biochem. Biophys. Res. Commun. 60:1 (1974).

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

[First Hit](#) [Fwd Refs](#)[Previous Doc](#) [Next Doc](#) [Go to Doc#](#)☐ [Generate Collection](#) [Print](#)

L2: Entry 17 of 23

File: USPT

Feb 13, 1996

DOCUMENT-IDENTIFIER: US 5490498 A

TITLE: Partial liquid breathing of fluorocarbons

Brief Summary Text (5):

Lung surfactant is composed of a complex mixture of phospholipid, neutral lipid and protein. Surfactant is roughly 90% lipid and 10% protein with a lipid composition of 55% dipalmitoyl diphosphotidylcholine (DPPC), 25% phosphatidylcholine (PC), 12% phosphatidylglycerol (PG), 3.5% Phosphatidylethanolamine (PE), sphingomyelin and phosphatidylinositol (PI).

[Previous Doc](#) [Next Doc](#) [Go to Doc#](#)

[First Hit](#) [Fwd Refs](#)[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

Generate Collection

Print

L2: Entry 11 of 23

File: USPT

Aug 3, 2004

DOCUMENT-IDENTIFIER: US 6770619 B2

TITLE: Lung surfactant compositions with dynamic swelling behavior

Brief Summary Text (6):

The constitution of a lung surfactant may vary with various factors such as species, age, and general health conditions of the subject. Various natural and synthetic constituents can substitute for each other in a surfactant. Therefore, even a non-rigorous definition of what the lung surfactant is and what should be included in a lung surfactant for therapeutic use is dependent on the situation. Surfactants isolated from lung lavage of healthy mammals contain about 10% protein (half of which is surfactant specific), and about 90% lipids, of which about 80% are phospholipids and about 20% are neutral lipids, including about 10% unesterified cholesterol. The phospholipid fraction contains mostly (about 76%) phosphatidylcholine (PC), about two thirds is dipalmitoyl phosphatidylcholine (DPPC), and the rest is unsaturated. About 11% of the phospholipids are made up of phosphatidylglycerol (PG), about 4% phosphatidylinositol, about 3% phosphatidylethanolamine, about 2% phosphatidylserine, about 1.5% sphingomyelin and about 0.2% lysophosphatidylcholine. Surfactant protein A (SP-A) represents 4% of surfactant and SP-B and SP-C and SP-D each make up less than 1%, according to current estimates.

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

[First Hit](#) [Fwd Refs](#)[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

End of Result Set

☐ [Generate Collection](#) [Print](#)

L4: Entry 16 of 16

File: USPT

May 19, 1998

DOCUMENT-IDENTIFIER: US 5753613 A

TITLE: Compositions for the introduction of polyanionic materials into cells

Detailed Description Text (21):

As noted above, the neutral lipid component in the liposomes is a lipid having two acyl groups, (i.e., diacylphosphatidylcholine and diacylphosphatidyl-ethanolamine). Lipids having a variety of acyl chain groups of varying chain length and degree of saturation are available or may be isolated or synthesized by well-known techniques. In general, less saturated lipids are more easily sized, particularly when the liposomes must be sized below about 0.3 microns, for purposes of filter sterilization. In one group of embodiments, lipids containing saturated fatty acids with carbon chain lengths in the range of C.sub.14 to C.sub.22 are preferred. In another group of embodiments, lipids with mono or diunsaturated fatty acids with carbon chain lengths in the range of C.sub.14 to C.sub.22 are used. Additionally, lipids having mixtures of saturated and unsaturated fatty acid chains can be used. Liposomes useful in the present invention may also be composed of sphingomyelin or phospholipids with other head groups, such as serine and inositol. Still other liposomes useful in the present invention will include cholesterol, diglycerides, ceramides, phosphatidylethanolamine-polyoxyethylene conjugates or phosphatidic acid-polyoxyethylene conjugates. Methods used in sizing and filter-sterilizing liposomes are discussed below.

Detailed Description Text (33):

Typical applications include using well known transfection procedures to provide intracellular delivery of DNA or mRNA sequences which code for therapeutically useful polypeptides. However, the compositions can also be used for the delivery of the expressed gene product or protein itself. In this manner, therapy is provided for genetic diseases by supplying deficient or absent gene products (i.e., for Duchenne's dystrophy, see Kunkel, et al., Brit. Med. Bull. 45(3):630-643 (1989), and for cystic fibrosis, see Goodfellow, Nature 341:102-103 (1989)). Other uses for the compositions of the present invention include introduction of antisense oligonucleotides in cells (see, Bennett, et al., Mol. Pharm. 41:1023-1033 (1992)).

Detailed Description Text (34):

Alternatively, the compositions of the present invention can also be used for the transfection of cells in vivo, using methods which are known to those of skill in the art. In particular, Zhu, et al., Science 261:209-211 (1993), incorporated herein by reference, describes the intravenous delivery of cytomegalovirus (CMV)-chloramphenicol acetyltransferase (CAT) expression plasmid using DOTMA-DOPE complexes. Hyde, et al., Nature 362:250-256 (1993), incorporated herein by reference, describes the delivery of the cystic fibrosis transmembrane conductance regulator (CFTR) gene to epithelia of the airway and to alveoli in the lung of mice, using liposomes. Brigham, et al., Am. J. Med. Sci. 298:278-281 (1989), incorporated herein by reference, describes the in vivo transfection of lungs of mice with a functioning prokaryotic gene encoding the intracellular enzyme, chloramphenicol acetyltransferase (CAT).

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

Refine Search

Search Results -

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L5 and otitis	0

Database:

US Pre-Grant Publication Full-Text Database
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 JPO Abstracts Database
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 IBM Technical Disclosure Bulletins

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END OF SEARCH HISTORY

[First Hit](#) [Fwd Refs](#)[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

Generate Collection

Print

L9: Entry 41 of 47

File: USPT

Jan 30, 2001

DOCUMENT-IDENTIFIER: US 6180142 B1

TITLE: Reduction of surfactant inactivation in pulmonary surfactant therapy

Detailed Description Text (16):

bLES (available from Biochemicals, Inc., London, Ontario, Canada): bovine lipid extract surfactant obtained by bovine lung lavage. This surfactant contains all of the phospholipids of natural surfactant plus SP-B and SP-C, but SP-A has been removed. The composition of the product is 79.2% phosphatidylcholine, 14.4% phosphatidylglycerol, 3% phosphatidylethanolamine, 2% sphingomyelin, 2% lysophosphatidylcholine, and trace amounts of lyso-bis-phosphatidic acid.

Detailed Description Text (18):

EXOSURF (available from Burroughs Wellcome, Research Triangle Park, N.C., USA). This is a protein-free surfactant containing 85% DPPC, 9% cetyl alcohol, and 6% tyloxapol (an ethoxylated-tert-octylphenol-polymethylene polymer).

CLAIMS:

7. A composition in accordance with claim 1 in which said surfactant is a synthetic, protein-free surfactant comprised of a member selected from the group consisting of phosphatidyl choline, dipalmitoyl phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, sphingomyelin, and lysophosphatidylcholine.

22. A method in accordance with claim 16 in which said surfactant is a synthetic, protein-free surfactant comprised of a member selected from the group consisting of phosphatidyl choline, dipalmitoyl phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine, sphingomyelin, and lysophosphatidylcholine.

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

[First Hit](#)[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

Generate Collection

Print

L12: Entry 6 of 7

File: PGPB

Jun 10, 2004

DOCUMENT-IDENTIFIER: US 20040110695 A1

TITLE: Immunotherapeutic methods and compositions

Detail Description Paragraph:

[0059] The principle phospholipid constituents of lamellar bodies are phosphatidylcholine (PC), sphingomyelin (SPH), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI) and lysolecithin (LPC). The phospholipid composition of lamellar bodies shows slight variation according to the cell of origin.

Detail Description Paragraph:

[0064] The presence of sphingoayelin in natural lamellar bodies and in the phospholipid vesicles claimed in the present invention is important. Sphingomyelin is not generally used, to our knowledge, in liposomes and serves to give flexibility and softness to lamellar bodies.

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)